AD_____

Award Number: DAMD17-03-2-0028

TITLE: A Randomized Placebo-Controlled Trial of Citalopram for Anxiety Disorders Following Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: Deborah L. Warden, M.D.

CONTRACTING ORGANIZATION: Henry M. Jackson Foundation for the Advancement of Military Medicine
Rockville, MD 20852

REPORT DATE: April 2005

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	April 2005	Annual (1 Apr 04 - 31 Mar 05)

4. TITLE AND SUBTITLE
A Randomized Placebo-Controlled Trial of Citalopram for Anxiety Disorders Following Traumatic Brain Injury

5. FUNDING NUMBERS
DAMD17-03-2-0028

6. AUTHOR(S)
Deborah L. Warden, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Henry M. Jackson Foundation for the Advancement of Military Medicine
Rockville, MD 20852

E-Mail: Deborah.Warden@na.amedd.army.mil

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 Words)

The overarching goal of this project is to study the effects of a serotonin reuptake inhibitor (SRI), citalopram, for the treatment of anxiety experienced by individuals after traumatic brain injury (TBI). Specifically, this project seeks to treat individuals who meet criteria for DSM-IV diagnosis of *Anxiety Disorder Due to a General Medical Condition,* within 6 to 24 months of TBI. A randomized placebo controlled design with 1-year follow-up will be utilized to evaluate the effectiveness of citalopram in alleviating significant anxiety symptoms that cause significant distress and can lead to medical retirement of active duty soldiers.

14. SUBJECT TERMS
No subject terms provided.

15. NUMBER OF PAGES
6

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Introduction:

The overarching goal of this project is to determine the effectiveness of citalopram for the treatment of anxiety disorders following Traumatic Brain Injury (TBI) and to examine possible longer term effectiveness of treatment with citalopram on symptom reporting and return to work/duty.

Body:

Participants who experienced a TBI 6 to 24 months ago and are experiencing anxiety are eligible for the study and if they agree to participate will sign informed consent prior to research tests and scales. An informational script is read to individuals. After the script is read, the individual will be given the informed consent to review. Patients will not be eligible to participate to participate in the study until they reach a Rancho Los Amigos level of 7 or 8. If there is any question as to a patient's capacity to consent, the neuropsychologist and/or psychiatrist involved in the study will assess the subject's intellectual and mental faculties prior to consent. Any confusional state prohibits a subject from being rated as a 7 or 8. After signing the informed consent, tests and scales will be administered and patients will be randomized to receive a 12-week course of citalopram or placebo. Female participants of childbearing potential will be given a serum pregnancy test. If test is positive, she will not be allowed to participate.

Eligible, consented participants will receive an increasing dose of citalopram or placebo up to a dose of 40 mg of citalopram or 4 pills of placebo. A blood sample drawn after completion of the 12-week treatment period will be used to obtain citalopram levels as a measure of medication compliance. A two-week taper will follow the treatment period. Study participants will receive comprehensive multidisciplinary evaluations at a DVBIC site, including neuropsychological and psychiatric interviews and evaluations at baseline, 12 weeks and 12 months. There have been no modifications made to the technical approach section of the protocol.

The number of subjects enrolled (or specimens used) in the study since last APR in the multi-center study is 1.

Since the last APR an addendum has been approved at Walter Reed Army Medical Center (WRAMC) that extends the study window. It has become clear over the last year with the increased number of patients sustaining TBI in OIF/OEF combat operations, that patients the DVBIC sees clinically are either very acutely injured or more than one year post injury. We are, therefore, concerned that we will miss a number of patients due to the 14 month cutoff. The 14 month cutoff was initially chosen arbitrarily and it has been determined that because we are examining a chronic post-TBI problem, 24 months is a

more appropriate cutoff point. The other 6 sites involved in the multi-center study have submitted or are in the process of submitting this addendum to their IRBs.

In regards to the recent attention given to SRI medications we have added information to the informed consent form alerting the participant that a history of depression may put him/her at an increased risk of suicide if he/she takes the study medication. This addendum was submitted and approved within the last year.

A lengthy contract processes between the Henry M. Jackson Foundation and the electronic data capture company and central pharmacy has caused substantial project delays. Our contract with LifeTree Technologies, Inc. was approved in July 2004 and our contract with the VA Clinical Research Pharmacy, Biomedical Research Institute of New Mexico (BRINM), was approved in September 2004. A drug handling procedure has been enacted and study drug shipment from the central pharmacy has arrived at WRAMC, San Diego National Naval Medical Center and the Hunter McGuire VA Hospital, and will be shipped to additional locations as they receive IRB approval and request medication. At the present time 6 of the 7 sites participating in this multi-center trial have received IRB approval and have begun actively recruiting. Additionally, as of 04 November 2004, our study web-site is activated and all study staff at WRAMC and all other sites in the multi-center study have been trained to use our electronic data capture system.

Recent literature on Escitalopram, the S-enantiomer from the racemic mixture that composes Citalopram, has suggested that the drug is effective in the treatment of Generalized Anxiety Disorder (GAD). Based on the merits of three placebo-controlled studies, Forest Laboratories announced the FDA approval of Escitalopram for the treatment of GAD in December of 2003 [Davidson J, et al., 2004; Forest Laboratories, 2003]. This new indication for the sister drug of Citalopram lends support to our hypothesis that Citalopram will help to reduce the symptoms of Anxiety Disorder Due to a General Medical Condition (TBI).

Reportable Outcomes:

There are no reportable outcomes from this study at the time of this submission.

Conclusions:

To date there has been 1 subject enrolled in the study, therefore there are no conclusions that can be made at this time.

References:

Davidson JR, Bose A, Korotzer A, Hongije Z. Escitalopram in the treatment of generalized anxiety disorder: Double-blind, placebo controlled, flexible-dose study. Depression & Anxiety. 2004;19(4):234-240.

Forest Laboratories. Press Release: Lexapro ™ receives FDA approval for the treatment of generalized anxiety disorder. December 2003. Accessed 14 Oct 2004 at: http://www.forestpharm.com.